

PGAM1 在胃癌诊治过程中有望成为一种新的治疗靶点,但其作用机制还需进一步研究。

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奥布卡因凝胶用于双腔气管导管插管对麻醉恢复质量的影响

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摘要 目的 观察盐酸奥布卡因凝胶用于双腔气管导管插管对麻醉恢复质量的影响。方法 择期行全身麻醉胸腔镜下肺大疱切除手术(手术时间 < 2h)患者 80 例, ASA I ~ II 级, 随机分成两组, 即石蜡油组(对照组, S 组)、盐酸奥布卡因组(试验组, A 组)。两组患者均行左侧双腔气管导管插管, S 组患者双腔气管导管前端 2/3 均匀涂抹石蜡油润滑, A 组患者双腔气管导管前端 2/3 均匀涂抹盐酸奥布卡因凝胶。记录两组患者在入室时(T_0)、手术结束前 5min(T_1)、苏醒即刻(T_2)、拔管即刻(T_3)、拔管后 1min(T_4)、拔管后 5min(T_5)、拔管后 10min(T_6)、出室时(T_7)等各时间点的心率(HR)、平均动脉压(MAP)、心率 × 收缩压(RPP); 观察患者在拔管期躁动、呛咳、屏气、声嘶的发生率, 拔管后即刻、拔管后 1h、拔管后 6h 的咽痛视觉模拟评分(VAS)及舒适度。结果 与 S 组比较, A 组的 HR、MAP、RPP 波动较小, 更加稳定; A 组躁动、声嘶发生率降低($P < 0.05$), A 组在拔管后即刻、拔管后 1h VAS 评分低于 S 组($P < 0.05$), A 组舒适度优于 S 组($P < 0.05$)。结论 盐酸奥布卡因凝胶涂抹双腔气管导管能够稳定麻醉恢复期血流动力学、降低拔管期并发症发生率, 提高患者舒适度, 改善麻醉恢复质量。

关键词 奥布卡因 双腔管 血流动力学 恢复质量

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Effect of Oxybuprocaine Gel on the Quality of Anesthesia Recovery with Double – lumen Endotracheal Intubation. Wu Hao, Tan Shigang, Cheng Pengfei, et al. Department of Anesthesiology, Central Theater Command General Hospital of the Chinese People's Liberation Army, Hubei 430070, China

Abstract Objective To observe the effects of oxybuprocaine hydrochloride gel on the quality of anesthesia recovery with double lumen endotracheal intubation. **Methods** Eighty (ASA I – II) patients underwent thoracoscopic bullous resection (surgical time < 2h) were randomly divided into two groups: paraffin oil group (control group, group S), oxybuprocaine hydrochloride group (test group, group A). Patients in both groups underwent left double – lumen endotracheal intubation. In group S, 2/3 of the double – lumen tube was uniformly coated with paraffin oil. In group A, 2/3 of the double – lumen tube was evenly coated with oxybuprocaine hydrochloride gel. Patient's Heart Rate (HR), Mean arterial pressure (MAP), Heart rate multiplied by Systolic blood pressure (RPP) were recorded at baseline (T_0), 5min before the end of surgery (T_1), immediately after awaking (T_2), extubation (T_3), 1min (T_4), 5min (T_5), 10min (T_6) after extubation and out of the room (T_7). Patient's agitation, cough, breath holding and hoarseness during the extubation period were also observed; Visual analogue score (VAS) and comfort degree were recorded immediately after extubation, 1h and 6h after extubation. **Results** Compared with S group, the fluctuation range of HR, MAP and RPP of group A was smaller and more stable, the incidence of agitation and hoarseness in group A was lower than that in group S, VAS score of group A was lower than that of group S immediately and 1h after extubation; also the comfort degree of group A was better than that of group S ($P < 0.05$). **Conclusion** Double – lumen endotracheal tube coated with oxybuprocaine gel can stabilize hemodynamics during recovery, reduce the incidence of complications during extubation, improve comfort degree and quality of anesthesia recovery.

Key words Oxybuprocaine; Double lumen; Hemodynamics; Recovery quality

双腔气管导管外径粗大,对气道的刺激易引起患者躁动、呛咳、屏气和血流动力学的剧烈波动,增加心脑血管病患者死亡风险,且拔管后易引发咽喉部疼痛、声嘶等并发症^[1-3]。盐酸奥布卡因凝胶是一种酯类局部麻醉药,其表面麻醉作用强,涂抹于黏膜表面或者涂抹于各种管道、扩张器表面与黏膜接触后起到麻醉作用,盐酸奥布卡因凝胶用于黏膜表面局部麻醉,4min起效,8min可得到充分的麻醉效果,单次涂抹持续药效40min以上^[4,5]。根据古德华等^[5]在临床使用的效果来看,其持续效果可达3h,这与笔者观察到的临床效果是一致的,笔者猜想可能是与涂抹在气管导管上的奥布卡因持续吸收有关。奥布卡因在动物实验结果的毒理上显示,皮下给药的LD50,大鼠为60mg/kg,家兔为30mg/kg。本研究观察了双腔气管导管前端2/3涂抹盐酸奥布卡因凝胶对短时间手术恢复期血流动力学、拔管并发症的发生情况以及患者舒适度的影响,报告如下。

资料与方法

1. 一般资料:本研究经笔者医院医学伦理学委员会讨论并批准研究方案,所有患者均签署麻醉知情同意书。选择2018年1~12月择期行胸腔镜下肺大疱切除术患者80例,手术时间<2h,患者年龄15~80岁,性别不限,ASA I~II级。排除标准:预期困难插管患者,操作中插管两次及以上者,手术时间>2h者,严重心脑血管病史、咽炎病史,术中发生严重麻醉及手术并发症者,语言沟通困难者。

2. 麻醉方法:术前常规禁饮禁食,入室建立外周静脉通道,麻醉诱导前补充晶体液250ml,常规连续监测心率(heart rate, HR)、无创血压(noninvasive blood pressure, NIBP)、心电图(electrocardiogram, ECG)、脉搏血氧饱和度(saturation blood pulse O_2 , SpO_2)、呼气末二氧化碳(end – tidal CO_2 partial pressure, $PetCO_2$)、气道压和潮气量(tidal volume, VT)。两组患者麻醉诱导药物和剂量一致:咪唑安定0.05mg/kg,舒芬太尼0.80 μ g/kg,依托咪酯0.30mg/kg,阿曲库铵0.25mg/kg,诱导5min后,脑电双频谱指数(bispectral index, BIS)值维持在40~60,行双腔管气管插管,均选用Robertshaw双腔支气管导管,男性35~37F、女性32~35F,经纤维支气管镜准确定位,连接呼吸机、调节呼吸参数,维持 $PetCO_2$ 在35~45mmHg(1mmHg=0.133kPa),BIS值维持在40~60。麻醉维持:丙泊酚4~8mg/(kg·h)、瑞芬太尼25~30 μ g/(kg·h)静脉泵注,阿曲库铵0.15mg/(kg·h)间断静脉注射。手术结束前30min给予舒芬太尼10 μ g术后镇痛,手术结束前15min停用阿曲库铵,手术结束前5min停用异丙酚,手术结束时停用瑞芬太尼。

3. 拔管指征:关胸后吸净气管内和口咽部分泌物,充分膨肺,待吞咽反射恢复,呼吸频率10~20次/分,潮气量>6ml/kg,脉搏氧饱和度(SpO_2)在吸空气时>95%,拔出双腔管,观察30min后,无特殊情况送回病房。

4. 观察指标:(1)记录入室时(T_0)、手术结束前

5min(T₁)、清醒即刻(T₂)、拔管即刻(T₃)、拔管后1min(T₄)、拔管后5min(T₅)、拔管后10min(T₆)、出室时(T₇)共8个时间点的心率(HR)、平均动脉压(MAP)、心率×收缩压(RPP正常值<12000,RPP与ECG II导联缺血性改变有一定关联,RPP>12000提示心肌缺血,RPP>15000可能发生心绞痛)的变化。(2)躁动发生率(苏醒期躁动评分:0分:合作且安静;1分:刺激时有挣扎,但无需按压;2分:无刺激时有挣扎,但无需按压;3分:挣扎剧烈,需多人按压。2分和3分视为苏醒期躁动)。(3)呛咳和屏气的发生率。(4)拔管后声音嘶哑发生率。(5)拔管后即刻、1h、6h咽喉痛视觉模拟评分(visual analogue score,VAS)。(6)患者的舒适度(采用患者主观舒适度量表评估,分为优、良、差3个等级,优、良视为舒适,差视为不舒适)^[6]。

5. 统计学方法:采用SPSS 25.0统计学软件对数据进行分析。计量资料以均数±标准差($\bar{x} \pm s$)表示,组间比较用独立样本t检验,组内不同时间点采用重复测量方差分析,计数资料采用 χ^2 检验,以 $P < 0.05$ 为差异有统计学意义。

结 果

1. 一般资料:本研究共入组病例80例,对照组40例,观察组40例。两组患者在性别构成、身高、年龄、体重等方面比较,差异无统计学意义($P > 0.05$),详见表1。

表1 两组患者一般情况比较 ($\bar{x} \pm s, n = 40$)

项目	A组	S组
男性	36	36
女性	4	4
年龄(岁)	27.6 ± 14.1	24.8 ± 13.7
身高(cm)	173.9 ± 6.7	174.0 ± 7.3
体重(kg)	58.0 ± 8.7	57.5 ± 7.5

2. 恢复期循环变化:组内比较,S组HR、MAP、RPP的组内两两比较,分别在T₁~T₃和T₁~T₃、T₅~T₆和T₁~T₃、T₅~T₆时间点比较差异有统计学意义($P < 0.05$),A组HR、MAP、RPP的组内两两比较,分别在T₁~T₂和T₁~T₂、T₄~T₅和T₁~T₂、T₅时间点比较差异有统计学意义($P < 0.05$)。组间比较,T₀时两组患者的HR、MAP、RPP比较差异无统计学意义($P > 0.05$),与S组比较,T₁、T₃~T₇时A组的HR低于S组,T₁、T₃~T₆时A组的MAP低于S组($P < 0.05$),T₁~T₇时A组的RPP均低于S组($P <$

0.05),A组的HR、MAP、RPP波动较S组小,详见图1、图2和图3。

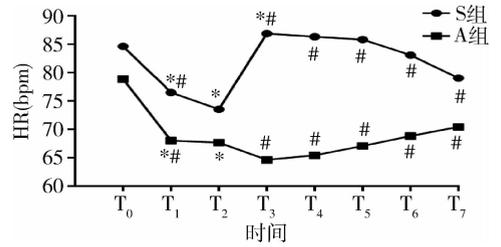


图1 两组不同时间点HR比较

组内两两比较,* $P < 0.05$;组间同时间点比较,# $P < 0.05$

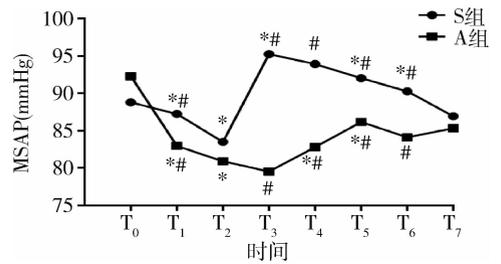


图2 两组不同时间点MAP比较

组内两两比较,* $P < 0.05$;组间同时间点比较,# $P < 0.05$

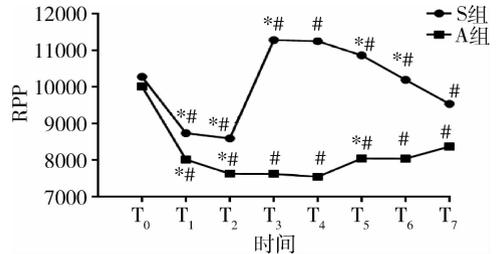


图3 两组不同时间点RPP比较

组内两两比较,* $P < 0.05$;组间同时间点比较,# $P < 0.05$

3. 恢复期躁动、屏气、呛咳、声嘶发生率比较:与S组比较,A组躁动、声嘶数明显少于S组($P < 0.05$),但呛咳和屏气组间比较,差异无统计学意义($P > 0.05$),详见表2。

表2 两组患者躁动、屏气、呛咳、声嘶发生率比较 [n(%)]

组别	n	躁动	屏气	呛咳	声嘶
A组	40	4(10.0)*	20(50.0)	15(37.5)	4(10.0)*
S组	40	12(30.0)	26(65.0)	21(52.5)	8(20.0)

与S组比较,* $P < 0.05$

4. 拔管后即刻、1h、6h咽喉痛VAS比较:与S组比较,A组在拔管后即刻、拔管后1hVAS低于S组

($P < 0.05$), 两组在拔管后 6h VAS 比较, 差异无统计学意义 ($P > 0.05$), 详见表 3。

表 3 两组患者拔管后即刻、1h、6h 咽喉痛

VAS 比较 ($\bar{x} \pm s$)

组别	n	拔管后即刻	拔管后 1h	拔管后 6h
A 组	40	1.70 ± 1.34 [*]	0.13 ± 0.40 [*]	0.03 ± 0.15
S 组	40	2.70 ± 1.26	0.63 ± 0.74	0.15 ± 0.36

与 S 组比较, ^{*} $P < 0.05$

5. 术后患者舒适度比较: 与 S 组比较, A 组舒适度例数明显增加, 差异有统计学意义 ($P < 0.05$), 详见表 4。

表 4 两组患者术后舒适度比较 [n (%)]

组别	n	舒适	不舒适
A 组	40	37(92.5) [*]	3(7.5) [*]
S 组	40	26(65.0)	14(35.0)

与 S 组比较, ^{*} $P < 0.05$

讨 论

临床中观察到, 气道各部位对气管导管刺激非常敏感, 这可能与气道内丰富的神经分布有关。在全身麻醉恢复期, 随着患者体内麻醉药物的代谢, 残留药物对气道中气管导管刺激的抑制作用越来越弱, 气管导管产生的刺激会引起循环系统的剧烈波动, 因此拔管期是心血管不良事件发生的高危期^[7,8]。麻醉苏醒过程中, 气管导管对气道的刺激和各种原因引起的咽喉声门部损伤, 会导致患者出现烦躁、呛咳、憋气、声嘶以及咽喉疼痛等症状, 并降低麻醉苏醒后舒适度^[6,9-11]。因此, 如何减少气管内和咽喉声门部的伤害性刺激传入, 降低循环的波动和拔管期并发症, 是麻醉医生需要考虑的临床问题。

既往研究表明, 局部麻醉药用于全身麻醉单腔气管插管能减少气道的刺激传入, 继而降低恢复期的并发症, 目前报道用于单腔气管插管的局部麻醉药有利多卡因、罗哌卡因、达克罗宁胶浆^[5,12-15]。Tung 等^[16]对可以预防气管插管全身麻醉后出现咳嗽、咽喉不适等并发症的药物进行系统评价和 Meta 分析, 有效的方法包括利多卡因[静脉内应用(IV)、气管内应用]、右美托咪定 IV、瑞芬太尼 IV 和芬太尼 IV。Gogus 等^[17]开展的一项前瞻性研究报道了应用右美托咪定可以降低气管插管和拔管期的血流动力学波动。Kim 等^[18]开展的一项随机对照试验研究表明, 右美

托咪定可以预防术后躁动和谵妄的发生。Kuriyama^[19]报道了术前静脉注射地塞米松可预防成人手术患者气管插管相关的咽喉痛。

随着肺隔离技术的发展, 使用双腔气管导管对肺进行隔离已成为胸外科手术的最佳选择之一, 双腔气管导管极大地方便了外科医生的手术操作, 但却给麻醉医生带来了挑战: 气管导管的管径粗、进入支气管、与气道接触范围大、术中术后多次支气管内吸引、拔出导管刺激强、循环影响大、插管技术及管理要求高、拔管期并发症多, 因此使用双腔气管导管更需要关注恢复期循环和拔管期并发症的发生情况^[3,20,21]。

随着麻醉理念的进步, 安全无痛舒适已是麻醉的基本需求, 因此研究需要采取较好的方法来减轻双腔气管插管给患者带来的不适, 经过比较, 笔者认为奥布卡因凝胶使用方便, 可以均匀涂抹在双腔气管导管上, 以便充分地与气管和咽喉声门部位接触, 起到良好的局部麻醉作用, 并且附着于气管导管上的凝胶可以持续吸收, 维持麻醉效果, 与液态类局部麻醉药相比有明显的优势。现有的凝胶类局部麻醉药包括利多卡因胶浆、达克罗宁胶浆, 与奥布卡因凝胶比较, 利多卡因黏膜穿透力差, 效果不及奥布卡因, 而达克罗宁属于芳酮型局部麻醉药, 具有刺激性, 患者耐受力差异较大, 不良反应明显, 药代动力学尚不清楚。综合比较, 研究选择了奥布卡因凝胶, 且目前尚无其在双腔气管导管中的应用报道。但奥布卡因可有过敏反应, 剂量过大、吸收过快可致中毒反应, 临床使用中需引起重视。

本研究中, 比较手术时间 $< 2h$ (双腔气管导管保留时间均在 3h 以内) 择期行双腔气管导管插管的手术, 分别在导管前端涂抹石蜡油和奥布卡因凝胶以观察麻醉恢复期循环、拔管期并发症以及麻醉苏醒后舒适度的情况, 结果提示, 通过组内各时间点的两两比较, 两组都有部分时间点之间的 HR、MAP、RPP 比较差异有统计学意义 ($P < 0.05$), 组间比较, 除了 T_0 时两组患者的 HR、MAP、RPP 比较差异无统计学意义 ($P > 0.05$), 其余几乎所有时间点 A 组的 HR、MAP、RPP 都较 S 组低 ($P < 0.05$), 不论是组内还是组间比较, A 组的 HR、MAP、RPP 波动幅度更小, 更加稳定, 笔者认为, 在组内因为有麻醉、拔管、吸痰等因素存在, 各时间点之间的 HR、MAP、RPP 难免会存在差异, 但是 A 组的波动幅度明显小于 S 组, 表明在奥布卡因的作用下, A 组的循环表现出了更小的波动, T_1 时, 两组间 RPP 比较差异有统计学意义, 表明即使

在麻醉状态下,奥布卡因也可以减轻气管导管对气管壁的刺激,从而起到稳定循环的作用,这与曾彦茹等^[12]、Fang等^[15]的研究结论是一致的,T₂~T₇两组间RPP比较差异有统计学意义,表明奥布卡因在拔管时降低应激反应、在拔管后气管壁持续的局部麻醉镇痛效果可以持续的稳定患者血流动力学, Lee等^[13]也对这一现象进行了报道。

奥布卡因凝胶均匀涂抹双腔气管导管,能在声门和气管内黏膜处更好地发挥局部麻醉和润滑的作用,减少了气管黏膜和咽喉声门部位神经末梢的刺激性传入,阻断了气管、咽喉声门部位刺激,降低了交感神经的兴奋性,同时有效抑制气管导管和吸痰刺激对交感肾上腺素髓质系统的激活,减少儿茶酚安的释放,从而阻断一系列的连锁反应,包括HR增快、MAP升高、心肌耗氧增加等,继而降低血流动力学的波动,对于并存有心脑血管疾病的患者是非常有益的^[3,5,8,9]。

A组躁动发生率、声嘶发生率、拔管后即刻VAS、拔管后1hVAS均低于S组($P < 0.05$),A组舒适度例数明显多于S组($P < 0.05$),这表明可能与奥布卡因凝胶润滑减轻在插管和拔管期对气道的损伤,麻醉作用减少气管黏膜和咽喉声门部位神经末梢的刺激性传入有关,继而表现出对双腔气管导管更加耐受,刘海恋等^[22]报道了不同气管导管润滑剂对全身麻醉患者术后咽喉不适的影响,表明润滑效果并不会减轻咽喉疼痛、降低声音嘶哑的发生率以及增加耐管,但局部麻醉药的药理学作用可以减轻咽喉疼痛和气管导管刺激,并减少呛咳发生、增加耐管、减少带管时声门的对抗性活动、减轻导管对声带的压迫以及继发的机械损伤,从而减轻炎症、水肿反应,降低声嘶发生率,同时患者躁动的发生率降低,麻醉苏醒后的舒适度增加^[19,20]。本研究中奥布卡因的涂抹量在10~20mg,标准是双腔气管导管前2/3均匀涂抹,笔者预估均匀涂抹量的药效持续时间在3~4h,至于更长时间的手术,则需要进一步研究用法和用量的问题^[5]。

综上所述,盐酸奥布卡因凝胶涂抹双腔气管导管在时间<2h手术能够稳定麻醉恢复期血流动力学、降低拔管期并发症发生率,提高患者舒适度,改善麻醉恢复质量。

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